

## **REMARKS**

This reply is responsive to the Non-Final Office Action dated March 3, 2010. Claims 1–11 and 17–22 are pending and under consideration. With this Amendment, claims 2, 3, 9, 10, and 16 are being amended, and no claims are being added or cancelled. The amendments of the claims and the various rejections raised in the Office Action are discussed in more detail, below.

### **I. The Amendments of the Claims**

Claims 2, 3, and 10 have been amended for conciseness and to remove the redundant recitation of substituents.

Claim 9 has been amended to correct an obvious typographical error.

Claim 16 has been amended to additionally recite the condition of osteoarthritis. Exemplary support for the amendment can be found, for example, in the specification as filed at pages 28–29 and 33.

No new matter is added by virtue of the amendments.

### **II. Rejections Under 35 USC §103(a)**

Claims 1–9, 11 and 17–22 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 00/07980 (“Brown”). The Examiner alleges that Brown teaches p38 kinase inhibitory amide compounds having cyclopropyl substituents.<sup>1</sup> Applicant respectfully traverses the rejection.

Determining obviousness under 35 U.S.C. § 103(a) requires an objective analysis involving four factual inquiries, which include (1) determining the scope and content of the prior art, (2) resolving the level of ordinary skill in the art, (3) ascertaining the differences between the claimed invention and the prior art, and (4) evaluating evidence of secondary factors, also known as objective indicia of non-obviousness. *See Graham v. John Deere Co.*, 383 US 1, 17-18, 148 USPQ 459 (1966). A claim composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. *See KSR International Co. v. Teleflex Inc.*, 550 US 398, 82

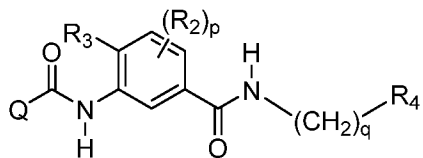
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<sup>1</sup> Office Action, pages 2–3.

USPQ2d 1385, 1385 (2007). “It is also important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *See id.*

Where the claims at issue involve a chemical compound, “a *prima facie* case of obviousness requires structural similarity between claimed and prior art subject matter ... where the prior art gives reason or motivation to make the claimed compositions.” *See Eisai Co., Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1357, 87 USPQ2d 1452 (Fed. Cir. 2008). Obviousness based on structural similarity can thus turn on the “identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (*i.e.* a lead compound) in a particular way to achieve the claimed compound.” *See Id*; *see also Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356, 83 USPQ2d 1169 (Fed. Cir. 2007) (emphasis added). Importantly, “post-KSR, a *prima facie* case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound.” *See Eisai Co., Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d at 1359 (emphasis added). The Examiner has failed to establish a *prima facie* case because neither of these requirements are met.

Brown discloses a broad class of compounds that inhibit p38 kinase activity, where the compounds have the structural formula on page 4 of WO 00/07980:



Brown recites a myriad of groups for the variables Q, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub>. For example, Brown states that Q can be aryl or heteroaryl which optionally bears 1, 2, 3 or 4 substituents; R<sub>3</sub> can be (1-6C)alkyl or halogeno; R<sub>2</sub> can be hydroxy, halogeno, trifluoromethyl, cyano, mercapto, nitro, amino, carboxy, 15 (1-6C)alkoxycarbonyl, (1-6C)alkyl, (2-6C)alkenyl, (2-6C)alkynyl, (1-6C)alkoxy, (1-6C)alkylamino or di-[(1-6C)alkyl]amino; and R<sub>4</sub> can be aryl, cycloalkyl, heteroaryl, a heterocyclyl, unsubstituted or substituted with a myriad of groups. The value for p can vary from 0 to 2, and q can vary from 0 to 4. In formulating the rejection, the Examiner selects values for Q, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, p and q substituents, and the substituents on Q to generate an unnamed compound that allegedly renders the claimed compounds obvious. However, the Examiner, does not point to any description in Brown for any particular suggestion or motivation for why particular substituents from the variable groups would be selected by the skilled artisan to arrive at the combination set forth in the Office Action.

On the nature of variable R<sub>4</sub> in the formula of Brown, the Office Action alleges that Brown discloses cyclopropyl groups. Although Brown does state that R<sub>4</sub> can be a cycloalkyl, the exemplary cycloalkyl groups in Brown have ring carbons of C<sub>4</sub> (e.g., cyclobutyl) or higher. See WO 00/07980, page 15, lines 7-10. The Examiner provides no reason in Brown that would lead a skilled artisan to select cycloalkyl for R<sub>4</sub> over the other possible groups for R<sub>4</sub>, e.g., aryl, heteraryl, or heterocyclyl, and further has failed to establish how those of ordinary skill in the art would be led specifically to R<sub>4</sub> being a cyclopropyl group when the exemplary cycloalkyl groups in Brown are C<sub>4</sub> or higher.

In essence, the Office Action has not set forth the *reasons* that would have prompted a person of ordinary skill in the art to select particular chemical groups as *identifiable, predictable* solutions from the myriad of substituents available for the compounds in Brown to arrive at the claimed compounds that have p38 kinase inhibitory activity. It is submitted that rather than being guided by Brown, the selections made by the Patent Office merely uses the substituent groups that are recited in the instantly pending claims. See *In re Wesslau*, 147 USPQ 391, 393 (CCPA 1965) (“It is impermissible within the framework of [a] section 103 [rejection] to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.”).

Further, as noted by the Federal Circuit in *Eisai Co., Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1359, 87 USPQ2d 1452 (Fed. Cir. 2008), “Obviousness based on structural similarity thus can be proved by identification of some motivation that would have led one of ordinary skill in the art to select and then modify a known compound (i.e. a lead compound) in a particular way to achieve the claimed compound.”<sup>2</sup> Here, we note that Brown discloses numerous exemplary compounds that inhibit p38 kinase activity, but the Office Action does not set forth what a lead compound a person of skilled in the art would select in Brown, the reasons why the skilled artisan would select such a compound, and the motivation that would lead a skill artisan to modify the lead compound to arrive at the claimed p38 kinase inhibitors.

With the failure to meet the requirements for establishing as case of *prima facie* obviousness, Applicant submits that the rejection under 35 U.S.C. § 103(a) should be withdrawn.

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<sup>2</sup> See also *Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356 (Fed. Cir. 2007).

### **Rejoinder of Claims**

In the Restriction Requirement dated October 1, 2009 (the "Restriction Requirement"), the Examiner indicated that withdrawn process claims which depend from an allowed composition claim or otherwise incorporate all limitations of an allowed composition claim would be rejoined. *See* Restriction Requirement, pages 8–9. Applicant respectfully submits that the composition claims are in condition for allowance, and that the withdrawn method claims, which depend from or otherwise contain all of the limitations of the allowed composition claims, should be rejoined and examined on the merits.

### **Conclusion**

In view of the foregoing, Applicant submits that the independent claims are allowable over the citations of record. Further, the dependent claims should also be allowable for the same reasons as their respective base claims. Separate and individual consideration of the dependent claims is respectfully requested.

An indication of allowance of all claims is respectfully solicited. In the event any issues remain, Applicant would appreciate the courtesy of a telephone call to their counsel to resolve such issues and place all claims in condition for allowance.

No fees are believed to be due in connection with this Amendment. However, the Director is authorized to charge any additional fees that may be required, or credit any overpayment, to Dechert LLP Deposit Account No. 50-2778 (**Order No.** 383299-336US (107322)).

Respectfully submitted,



Date: June 3, 2010

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